Taiwanese Journal of Obstetrics & Gynecology 54 (2015) 722–725

Contents lists available at ScienceDirect

Taiwanese Journal of Obstetrics & Gynecology

journal homepage: www.tjog-online.com

Original Article

Application of the World Health Organization Fracture Risk Assessment Tool to predict need for dual-energy X-ray absorptiometry scanning in postmenopausal women

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ARTICLE INFO

Article history:
Accepted 5 May 2015

Keywords:
bone mineral density
dual-energy X-ray absorptiometry
Fracture Risk Assessment Tool
osteoporosis
vertebral fracture assessment

ABSTRACT

Objective: To evaluate the efficacy of the World Health Organization Fracture Risk Assessment Tool, excluding bone mineral density (pre-BMD FRAX), in identifying Taiwanese postmenopausal women needing dual-energy X-ray absorptiometry (DXA) examination for further treatment.
Materials and methods: The pre-BMD FRAX score was calculated for 231 postmenopausal women who participated in public health education workshops in the local Keelung community, Taiwan. DXA scanning and vertebral fracture assessment (VFA) were arranged for women classified as intermediate or high risk for fracture using the pre-BMD FRAX fracture probability.
Results: Pre-BMD FRAX classified 26 women as intermediate risk and 37 as having high risk for fracture. Subsequent DXA scans for these 63 women showed that 36 were osteoporotic, 19 were osteopenic, and eight had normal bone density. Concurrent VFA revealed 25 spine factures in which 14 were osteoporotic, seven were osteopenic, and four had normal bone density. The efficacy of the pre-BMD FRAX score to identify those patients with low bone mass by DXA was 87.3% (55/63). When VFA was combined with BMD to identify those patients with high risk (osteopenia, osteoporosis, or spinal fracture), the efficacy of the pre-BMD score increased to 93.7% (59/63). According to the National Osteoporosis Foundation, the overall concordance between pre-BMD FRAX and BMD, expressed through the kappa index, was 0.967. Compared with the evaluation when BMD was used alone, there was a significant increase in efficacy in identifying women who need treatment using BMD plus VFA or FRAX plus BMD. Furthermore, the highest efficacy was achieved when FRAX with BMD and VFA was used.
Conclusion: The pre-BMD FRAX score not only efficiently predicts postmenopausal patients who are potentially at risk and might require treatment but also reduces unnecessary DXA use. Concurrent VFA during DXA use increases spine fracture detection. This improvement in diagnostic efficacy allows clinicians to provide the most appropriate therapeutic recommendation.

Introduction

Osteoporosis is defined as a skeletal disorder characterized by compromised bone strength, predisposing a person to an increased risk of fracture [1]. Most cases of osteoporosis occur in postmenopausal women due to estrogen deficiency. Because osteoporotic fractures in the spine and hip are associated with substantially high morbidity and mortality, osteoporosis has become a serious health threat for elderly women. Thus, it is important to identify postmenopausal women who have low bone mass and high fracture risk to provide preventive and pharmacologic therapy.

Bone mineral density (BMD) is the most common measurement used to evaluate bone strength. Dual-energy X-ray absorptiometry

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http://dx.doi.org/10.1016/j.tjog.2015.10.005

(DXA) has been established by the World Health Organization (WHO) as a technique of reference for assessing BMD in postmenopausal women [2]. The most pivotal treatment guidelines, for example, the National Osteoporosis Foundation (NOF) treatment guideline [3], or studies also utilized the DXA T-score classification and a clinical history of vertebral or hip fractures to define the entry criteria. The North American Menopause Society recommends that BMD should be used in women aged 65 years or older and postmenopausal women with medical causes of bone loss, additional risk factors, or a fragility fracture [4]. However, it has been reported that a larger population burden of fracture occurred in people with osteopenia compared to those with osteoporosis [5]. From a healthcare perspective, fracture prevention should not depend only on DXA testing.

Besides estrogen deficiency, there are many risk factors associated with osteoporotic fractures in postmenopausal women [4,6]. The WHO has developed a registered web-based clinical scale assessing Fracture Risk Assessment Tool (FRAX) that integrates an individual's risk factors and reports the 10-year probability of hip or other major osteoporotic fracture [7,8]. FRAX can be calculated with or without hip BMD and has provided both intervention thresholds for treating osteoporosis and assessment thresholds for the use of DXA.

It has been reported that up to half of all vertebral fractures are not diagnosed [9]. It is well established that the existence of a previous vertebral fracture increases the risk of subsequent fractures, regardless of BMD. Greenspan et al [10] reported that in long-term care residents, FRAX, based on femoral neck bone density alone, identified 81% of participants for treatment but missed almost 10% of women with silent vertebral fractures that might benefit from treatment. Thus, the identification of a vertebral fracture significantly alters treatment decisions and considerations.

The aim of this study was to assess the efficacy of pre-BMD FRAX scores in identifying postmenopausal women who need DXA measurement for further treatment. In addition, this study also evaluated the use of concurrent vertebral fracture assessment (VFA) during DXA to improve osteoporosis risk detection.

Materials and methods

Study design

From January 2012 to June 2013, public health education workshops and clinical services were held in the local community of Keelung. A total of 231 postmenopausal women were enrolled in the WHO pre-BMD FRAX evaluation. The enrollment criteria for DXA and VFA examination were patients with intermediate FRAX fracture risk (10–20% probability for major osteoporotic fracture or 1.5–3% for hip fracture) and high risk (≧20% probability for major osteoporotic fracture or ≧3% for hip fracture). The study was approved by the Chang Gung Memorial Hospital Ethical Medicine Committee.

FRAX score

FRAX scores were calculated with an online tool using the Taiwan algorithm [7]. In brief, completion of 12 fields were required, which included age (years); sex (male or female); height (cm); weight (kg); history of previous fracture (defined as a fracture in adult life occurring spontaneously, or arising from trauma which, in a healthy individual, would not have resulted in a fracture); history of parental hip fracture; current smoking; glucocorticoids exposure (defined as current exposure or previous oral glucocorticoid exposure for >3 months, with a dose of 5 mg prednisolone daily or more); diagnosis of rheumatoid arthritis; secondary osteoporosis [including type I (insulin-dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition or malabsorption, and chronic liver disease]; daily alcohol intake of more than three units; and femoral neck DXA score (in g/cm^2 or T score based on the National Health and Nutrition Examination Survey III female reference data).

The FRAX scores were calculated first using clinical factors alone and were then reassessed with the inclusion of BMD (g/cm^2) of femoral neck.

BMD measurement and VFA

BMD of the hip (total hip, femoral neck) and posterior–anterior spine (L1–L4) were measured by DXA scanning (GE-Lunar, iDAX, Madison, WI, USA) installed at Keelung Chang Gung Memorial Hospital. WHO guidelines were used to define BMD: a T score of ≧−1 denotes normal bone; a T score between −1 and −2.5 denotes osteopenia, and a T score of ≦−2.5 denotes osteoporosis. After BMD measurement, the presence of vertebral fractures in the thoracic or lumbar spine was determined by VFA with DXA scanning simultaneously. VFA assesses T3–L4 vertebral fractures and classifies them according to Genant's criteria of mild, moderate, and severe vertebral fractures [11].

Statistical analysis

The levels of agreements between BMD and FRAX + BMD, BMD and BMD + VFA, and BMD and FRAX + BMD + VFA were assessed using kappa statistic and Fisher exact test. Positive predictive value (PPV) and negative predictive value (NPV) of NOF treatment guideline [3] for pre-BMD FRAX, BMD, FRAX, BMD with VFA, and FRAX with VFA were also calculated.

Results

A total of 63 patients (aged 48–81, mean age 66.2 years), who were identified from pre-BMD FRAX, were enrolled. According to the pre-BMD FRAX scores, 26 patients were classified as intermediate risk and 37 were classified as high risk for fracture. Clinical risk factors evaluated by FRAX are shown in Table 1.

BMD and VFA of DXA scans were performed and evaluated by a radiology specialist (Dr YC Lin). Results of DXA examination ($n = 63$) showed that 36 (57%) were osteoporotic, 19 (30.2%) were osteopenic, and eight (12.7%) were normal for bone density. VFA evaluation ($n = 63$) showed that 25 patients had spine fracture (Table 1). Of the 25 patients with spinal fractures, 14 were previously deemed to be osteoporotic, seven were osteopenic, and four were identified from the eight patients with normal bone density by DXA. From the results of the BMD alone, the efficacy of the pre-BMD FRAX score to identify the patients with low bone mass [osteoporosis ($n = 36$) or osteopenia ($n = 19$)] by DXA was 87.3% (55/63). Furthermore, when both BMD and VFA were used, the efficacy of the pre-BMD FRAX score increased to 93.7% (59/63) in identifying high-risk patients (osteopenia, osteoporosis, or spinal fracture).

According to the NOF treatment guideline [3], treatment is recommended for patients with the following conditions: hip or vertebral (clinical or asymptomatic) fractures, T scores of −2.5 or less at the femoral neck, total hip, or lumbar spine by DXA, postmenopausal women and men aged 50 and older with osteopenia (T score between −1.0 and −2.5) at the femoral neck, total hip, or lumbar spine by DXA, and a 10-year hip fracture probability of 3% or more or a 10-year major osteoporosis-related fracture probability of 20% or more based on the WHO absolute fracture risk model

Table 1
Description of clinical predictors used in the WHO Fracture Risk Assessment Tool (FRAX).

Clinical data/predictor	Postmenopausal women ($N = 63$)	Pre-BMD FRAX score ($N = 63$)	
	N (%) unless otherwise noted	High risk ($N = 37$)	Intermediate risk ($N = 26$)
Age (y)			
<65	27 (42.9)	4	23
65–75	25 (39.7)	22	3
>75	11 (17.5)	11	0
Body weight (kg)	55.7 ± 10.2	53.9 ± 10.2	58.3 ± 11.0
Body height (cm)	152.7 ± 5.9	151.0 ± 5.48	155.0 ± 5.74
History of fracture	7 (11.1)	5 (13.5%)	2 (7.7%)
Parental history of fracture	2 (3.2)	1 (2.7%)	1 (3.8%)
Current smoking	4 (6.3)	1 (2.7%)	3 (11.5%)
Three or more alcoholic beverages/d	1 (1.6)	0 (0%)	1 (3.8%)
Rheumatoid arthritis	0 (0)	0 (0%)	0 (0%)
Glucocorticoid use	1 (1.6)	0 (0%)	1 (3.8%)
Secondary osteoporosis	23 (36.5)	15 (40.5%)	8 (30.8%)
DXA			
T score ≤ -2.5[a]	36	25	11
$-2.5 \leq$ T score ≤ -1	19	10	9
$-1 \leq$ T score	8	2	6
Spine fracture by VFA	25	21	4

BMD = bone mineral density; DXA = dual-energy X-ray absorptiometry; FRAX = Fracture Risk Assessment Tool; VFA = vertebral fracture assessment; WHO = World Health Organization.
[a] T score is bone mineral density in the hip and lumbar spine by DXA.

(FRAX). The treatment/reassurance assignment from pre-BMD FRAX scores showed a strong consensus with that from BMD examination [kappa = 0.967, 95% confidence interval (CI) 0.904–1.031]. The PPV of treatment assignment by the FRAX score was 97.3% in predicting treatment assignment by BMD results. Alternatively, the NPV was 100% (Table 2).

In Table 3, in addition to PPV and NPV, use of BMD to identify patients who need treatment showed fair concordance with the use of FRAX with BMD (kappa = 0.7656, 95% CI 0.6064–0.9247), use of BMD combined with VFA (kappa = 0.6244, 95% CI 0.4375–0.8113), and use of FRAX with BMD and VFA (kappa = 0.5149, 95% CI 0.3189–0.7108). However, the efficacy of these methods in detecting osteoporosis was very different. Based on the aforementioned treatment guideline, there was a 57.1% (36/63) efficacy in identifying high-risk patients needing treatment when only BMD was used, 68.3% (43/63) when FRAX (including femoral neck BMD) was used, and 74.6% (47/63) when BMD combined with VFA was used. Furthermore, the efficacy of identifying high-risk patients needing treatment was 79.4% (50/63) when FRAX with VFA was used. These results also expose that if these patients only underwent bone density criterion evaluation, 11 (7 osteopenic and 4 normal, assessed by BMD) of 25 patients (44%) with spine fractures would go undetected.

Table 2
Agreement between pre-BMD FRAX scores and BMD study in treatment recommendation.

		BMD, n		Total	
		Treatment	Reassurance		
Pre-BMD FRAX score, n	Treatment	36	1	37	PPV = 97.3%
	Reassurance	0	26	26	NPV = 100%
	Total	36	27	63	

Kappa value = 0.967, standard error of kappa = 0.032 (95% CI: 0.904–1.031).
BMD = bone mineral density; FRAX = Fracture Risk Assessment Tool; NPV = negative predictive value; PPV = positive predictive value.

Discussion

The application of DXA is limited because it is nonportable, expensive, and time consuming. A number of clinical risk factors that provide information on fracture risk over that given by DXA were reported [12]. To increase the cost effectiveness of DXA, the clinical criteria of the FRAX score alone may also be useful in predicting patients who need DXA scans. This study demonstrated that the pre-BMD FRAX score is highly correlated with the incidence of osteoporotic patients as detected by DXA and as such may be considered as an alternative screening strategy to identify eligible patients in the community without DXA equipment. Although such efficacy is encouraging, several factors regarding these results still warrant further examination.

In this study, the efficacy of the pre-BMD FRAX score to identify those patients with low bone mass through DXA use was 87.3%, which increased to 93.7% after assessment with BMD combined with VFA. These results confirm that the use of pre-BMD FRAX to identify intermediate and high-risk patients can reduce unnecessary DXA scanning. Moreover, it can be used as assessment thresholds [8] to decide if DXA is needed. BMD alone is not optimal for detection in individuals with high risk of fracture [13–15]. Several reports have revealed that the evaluation of clinical risk factors that partially or totally contribute to fracture risk, independent of BMD, have improved fracture prediction [16–20]. In this study, only 57.1% of these women were found to need treatment when DXA was used alone. However, when both FRAX and DXA were used, the percentage of women identified to need treatment increased to 68.3%. Furthermore, the PPV of treatment assignment by the pre-BMD FRAX score was 97.3% and the NPV was 100%. Because the strength of agreement between pre-BMD FRAX and BMD is encouraging (kappa = 0.967, 95% CI 0.904–1.031), we confirmed that the pre-BMD FRAX score is a suitable method to identify not only those patients who need DXA evaluation but also those who require therapy. Similar results have been reported in patients with inflammatory bowel disease, in which the clinical FRAX score alone, compared with the FRAX score that included BMD, had a sensitivity of 100% and an NPV of 100% in identifying those patients needing DXA measurement or preventive treatment [21]. However, there were also some limitations in this study. In addition to a small number of enrolled patients, no DXA data for patients with low risk of FRAX score were available. Thus, the true accuracy of the pre-BMD FRAX score could not be determined.

Vertebral fracture is the hallmark of osteoporosis. The incidence of vertebral fracture is estimated to be approximately 10–15% among women aged 50–59 years and increased to 50% for women aged 80 years or more [22]. Radiologic imaging is required for the detection of vertebral fractures but only approximately one third of vertebral fractures are clinically apparent [23]. The specific criteria to be used to select patients for spine imaging are still controversial. In this study, VFA and BMD were performed concurrently during DXA use. The efficacy of the pre-BMD FRAX score to identify patients with high risk increases from 87.3% (with BMD only) to 93.7% (BMD combined with VFA). The efficacy of the pre-BMD FRAX score also increases from 68.3% (FRAX including BMD) to 79.4% (FRAX and VFA) when identifying patients needing treatment. If these patients were evaluated only using BMD, 11 (7 osteopenic and 4 normal during BMD) of 25 patients (44%) with spinal fractures would have been missed. Similar results were also reported by El Maghraoui et al [24], in which 16% of the women with osteopenia and 8.5% of the women with normal BMD who may have not been identified as being at greater fracture risk were found to have unappreciated evident spinal fracture. The calculated kappa value and PPV between BMD and FRAX + BMD + VFA were lower than the results from other analyses. Therefore, it further confirms that the

Table 3
Kappa index value between BMD and FRAX with BMD, BMD combined with VFA, or FRAX with BMD and VFA.

		BMD, $n = 63$						
	NOF[a]	Treatment	Reassurance	Total	Kappa value (standard error, 95% CI)	PPV (%)	NPV (%)	Fisher exact test
FRAX + BMD	T	36	7	43	0.77 (0.08, 0.61–0.92)	83.7	100	6.584×10^{-11}
	R	0	20	20				
BMD + VFA	T	36	11	47	0.62 (0.10, 0.44–0.81)	76.6	100	3.56×10^{-8}
	R	0	16	16				
FRAX + BMD + VFA	T	36	14	50	0.51 (0.10, 0.32–0.71)	72.0	100	1.92×10^{-6}
	R	0	13	13				

BMD = bone mineral density; FRAX = Fracture Risk Assessment Tool; NOF = National Osteoporosis Foundation; NPV = negative predictive value; PPV = positive predictive value; VFA = vertebral fracture assessment.
[a] 2008 National Osteoporosis Foundation guidelines.

evaluation of high-risk patients should also include both clinical risk factors and VFA, in addition to BMD. Moreover, this study also demonstrates that concurrent use of VFA during DXA is a creditable method to diagnose spine fractures in postmenopausal women.

In conclusion, pre-BMD FRAX can efficiently predict those patients needing treatment to reduce unnecessary DXA. Therefore, pre-BMD FRAX may be applied in the community as well as in general outpatient clinics. Furthermore, the addition of VFA during DXA measurement can increase the diagnostic accuracy of vertebral fracture detection and provide the most appropriate therapeutic recommendation.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

Acknowledgments

The authors thank Kuo-Su Chen, MD (Department of Nephrology, Keelung Chang Gung Memorial Hospital), for his valuable statistical advice and Ingrid Ying-Yu Chern (intern, School of Medicine, Kaohsiung Medical University) for editing our manuscript.

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